Patent Claims

1. Process for preparing of the complete gp190/MSP1 protein of Plasmodium, in particular Plasmodium falciparum characterized in that the complete gene for gp190/MSP1 is expressed in a suitable system, preferably a host organism.

2. Recombinant manufacturing process according to Claim 1, characterized in that the synthesis of the DNA sequence on which the protein is based derives from the DNA sequence of the P. falciparum strain FCB-1.

3. Recombinant process according to Claim 2, characterized in that the AT content of the DNA sequence expressed is reduced compared to that of the naturally occurring sequence, preferably from 74% to 55%.

4. Recombinant process according to one or more of claims 1 to 3, characterized in that the gene on which the protein produced is based codes for the complete amino-acid sequence including signal peptide and attachment signal.

5. Recombinant process according to one or more of claims 1 to 3, characterized in that the gene on which the protein produced is based codes for the complete amino-acid sequence except for the attachment signal.

6. Recombinant process according to one or more of claims 1 to 3, characterized in that the gene on which the protein produced is based codes for the complete amino-acid sequence except for the attachment signal and the signal peptide.

7. Recombinant process according to one or more of claims 1 to 6, characterized in that it includes the following steps:

   (a) Design of the DNA sequence from P. falciparum FCB-1 to be synthesized, by which a DNA sequence with the codon frequencies common in the human

genome and maintaining the amino-acid sequence of the FCB-1 protein would be produced,

(b) division of the planned sequence into overlapping regions, preferably regions p83, p31, p36, gp30 and gp19,

(c) synthesis of desoxyoligonucleotides, each of them extending the whole length of a region,

(d) synthesis of the regions coding for gp19, gp30, p36 and p31 by PCR and synthesis of the region coding for p83 by fusion of two sequences comprising approximately 1200 bp,

(e) individual cloning of coding sequences,

(f) fusion of the complete gene and

(g) expression in a suitable expression system.

8. Recombinant process according to Claim 7, characterized in that the desoxyoligonucleotides synthesized in step (c) should be on average 120 nucleotides long and in each instance overlap the neighbouring sequences by about 20 bases.

9. Recombinant process according to one or more of Claims 1 to 8, characterized in that dPS56, RBSII is used as expression vector.

10. Recombinant process according to one or more of Claims 1 to 8, characterized in that pBi-5 is used as expression vector.

11. Recombinant process according to one or more of Claims 1 to 8, characterized in that ppTMCS is used as expression vector.

12. Recombinant process according to one or more of Claims 1 to 11, characterized in that the DNA sequence on which the protein is based is expressed in E. coli.

13. Recombinant process following Claim 12, characterized in that the E.coli strain used is the repressor-producing strain E. coli DH5alphaZ1.

14. Recombinant process according to one or more of Claims 1 to 11, characterized in that the DNA sequence on which the protein is based is expressed in HeLa cells.

15. Recombinant process according to one or more of Claims 1 to 11, characterized in that the DNA sequence on which the protein is based is expressed in CHO cells.

16. Recombinant process according to one or more of Claims 1 to 11, characterized in that the DNA sequence on which the protein is based is expressed in Toxoplasma gondii or Leishmania.

17. Complete DNA sequence, suitable for expression, of the gp190/MSP1 surface protein of Plasmodium, in particular P. faciparum, preferably obtainable through the recombinant process according to one or more of Claims 1 to 16.

18. DNA sequence, suitable for expression, according to Claim 17, characterized in that it does not code for the attachment signal.

19. DNA sequence, suitable for expression, according to Claim 18, characterized in that it codes neither for the attachment signal nor the signal peptide.

20. DNA sequence, suitable for expression, according to Claim 19, characterized in that it includes a sequence for 11 additional amino-acids, of which 6 are histidines, present at the N-terminus.

21. DNA sequence, suitable for expression, according to one or more of Claims 17 to 20, characterized in that the sequence includes no recognizable "splice donor" and "splice acceptor" signals.

22. DNA sequence, suitable for expression, according to one or more of Claims 17 to 21, characterized in that the sequence includes no large GC-rich sequences.

23. DNA sequence, suitable for expression, according to one or more of Claims 17 to 22, characterized in that the sequence includes no recognition signals for restriction enzymes recognizing sequences of six or more base pairs.

24. DNA sequence, suitable for expression, according to one or more of Claims 17 to 23, characterized in that the sequence for recognition signals of particular restriction nucleases in regions which, after processing of the protein, separate existing domains, contains uniquely occurring cleavage sites for restriction endonucleases.

25. DNA sequence, suitable for expression, according to one or more of Claims 17 to 24, characterized in that the sequence has at both its ends cleavage sites for endonucleases which do not appear in the remaining sequence and in a vector for use.

26. Host organism which contains the complete nucleic acid sequence for the gp190/MSP1 surface protein and/or the complete protein.

27. Host organism according to Claim 26, characterized in that the organism is E. coli.

28. Host organism according to Claim 27, characterized in that the E. coli strain is the repressor-producing E. coli strain DH5alphaZ1.

29. Host organism according to Claim 26, characterized in that the host organism is HeLa cells.

30. Host organism according to Claim 26, characterized in that the host organism is CHO cells.

31. Host organism according to Claim 29 or 30, characterized in that the host cells synthesize constitutively tTA.

32. Host organism according to Claim 26, characterized in that the hosts provided are Toxoplasma gondii, Leishmania, baculoviruses, adenoviruses or yeasts.

33. Use of a gp190/MSP1 protein manufactured according to Claims 1 to 16 for active immunization against malaria.

34. Use of a gp190/MSP1 protein manufactured according to Claims 1 to 16 for the manufacture of monoclonal antibodies suitable for passive immunization.

35. Use of a DNA sequence manufactured according to Claims 1 to 16 for the manufacture of a vaccine based on nucleic acids.

36. Process for stabilization of gene sequences, characterized in that the AT content of the sequence is reduced.

37. ~~36.~~ Stabilized gene, characterized in that it shows a reduced AT content than the unstabilized gene.

38. ~~37.~~ Vector containing a DNA sequence following one of the Claims 17 to 25 and/or ~~36~~ 37.

39. ~~38.~~ Host cells containing a vector according to Claim ~~37~~ 38.

40. ~~39.~~ Vaccine containing a protein manufactured according to a process according to any of the Claims 1 to 16 and/or a DNA sequence according to one of the Claims 17 to 25 and/or a host according to one of the Claims 26 to 32 and/or a vector according to Claim ~~37~~ 39.

41. Vaccine according to Claim 40, characterized in that it contains further immunity-promoting products from Plasmodium, especially P. falciparum.